

Amendments to the Claims:

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-2 (Cancelled)

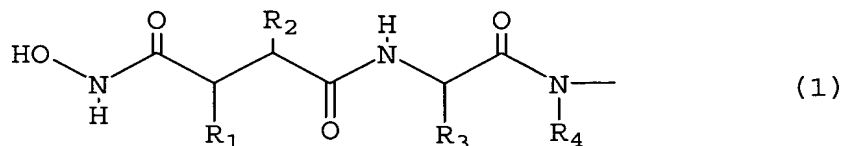
3 (Currently Amended). The ~~conjugate~~method of claim ~~1~~17, wherein the therapeutic agent for joint diseases is a matrix metalloprotease inhibitor.

4 (Cancelled)

5 (Currently Amended). The ~~conjugate~~method of claim 3, wherein the weight ratio of the matrix metalloprotease inhibitor to the entire conjugate is 0.01 to 50%.

6 (Currently Amended). The ~~conjugate~~method of claim 3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue.

7 (Currently Amended). The ~~conjugate~~method of claim 3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue represented by the general formula (1):



wherein

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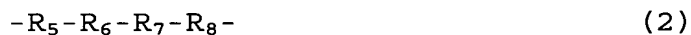
R₁ is a hydrogen atom, a hydroxyl group or a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₂ is a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₃ is a straight chain or branched alkyl group having 1 to 8 carbon atoms which may be substituted with a cycloalkyl group, an aryl group or a heterocyclic group; and

R₄ is a hydrogen atom or an alkyl group having 1 to 4 carbon atoms.

8 (Currently Amended). The ~~conjugate~~ method of claim ±17, wherein the spacer is represented by the general formula (2):



wherein

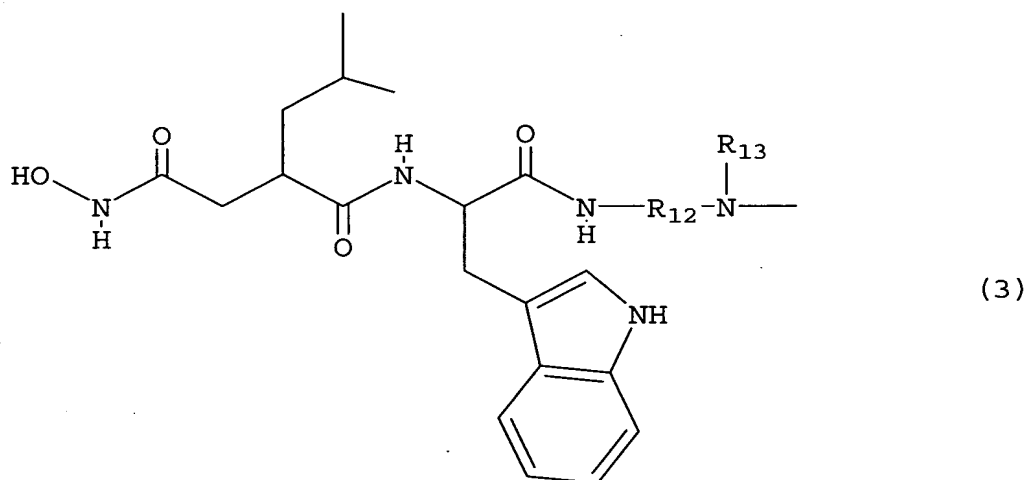
R₅ is a straight-chain or branched-chain alkylene group having 1 to 8 carbon atoms;

R₆ is an oxygen atom or a methylene or imino group which may be substituted with a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms;

R₇ is a straight-chain or branched-chain alkylene group having 1 to 10 carbon atoms into which one to three oxygen atoms may be inserted; and

R_8 is an oxygen atom, a sulfur atom or NR_9 , wherein R_9 is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

9 (Currently Amended). The ~~conjugate~~ method of claim 3, wherein the matrix metalloprotease inhibitor and the spacer constitute a moiety represented by the general formula (3):



wherein

R_{12} is a straight-chain or branched-chain alkylene group having 2 to 23 carbon atoms into which one imino group and/or one to four oxygen atoms may be inserted; and

R_{13} is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

10 (Currently Amended). The ~~conjugate~~ method of claim 3, wherein the matrix metalloprotease inhibitor in the form of a conjugate with hyaluronic acid, a hyaluronic acid

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derivative or a salt thereof inhibits a matrix metalloprotease *in situ*.

11 (Currently Amended). A method for preparing ~~the~~
a conjugate of (1) at least one therapeutic agent for joint
diseases which is bonded via a spacer to (2) hyaluronic acid,
a hyaluronic acid derivative or a salt thereof, wherein a
carboxyl group of the hyaluronic acid, derivative or salt, and
an amino group of the spacer form an amide bond, ~~of claim 1~~
comprising binding a site of the therapeutic agent for joint
diseases that does not affect the activity of the agent to a
~~carboxyl group of the~~ hyaluronic acid, a hyaluronic acid
~~derivative or a salt, thereof via a~~ the spacer.

12-16 (Cancelled)

17 (Currently Amended). A method for treating a
patient having a joint disease comprising administering to the
patient a pharmaceutical composition containing, as the
effective ingredient, a pharmaceutically effective amount of
~~the~~ a conjugate of (1) at least one therapeutic agent for
joint diseases which is bonded via a spacer to (2) hyaluronic
acid, a hyaluronic acid derivative or a salt thereof, wherein
a carboxyl group of the hyaluronic acid, derivative or salt,
and an amino group of the spacer form an amide bond ~~any one of~~
~~claims 1, 3, 5 10, 18, 19, 23 and 24 as the effective~~
~~ingredient to the patient.~~

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18 (Currently Amended). The ~~conjugate~~ method of claim ~~17~~, wherein the therapeutic agent for joint diseases is selected from the group consisting of a cyclooxygenase 2 inhibitor, an antirheumatic agent and a matrix metalloprotease inhibitor.

19-21 (Cancelled)

22 (Currently Amended). A method of treating a joint disease in a patient in need thereof, comprising administering a pharmaceutical composition to said patient in an amount sufficient for said treatment, wherein said pharmaceutical composition comprises a conjugate of (1) at least one therapeutic agent for joint diseases which is bonded via a spacer to (2) hyaluronic acid, a hyaluronic acid derivative or a salt thereof, wherein a carboxyl group of the hyaluronic acid, derivative or salt, and an amino group of the spacer form an amide bond ~~in accordance with claim 1~~.

23 (Currently Amended). The ~~conjugate~~ method of claim ~~17~~, wherein component (1) is a single therapeutic agent for joint disease.

24 (Currently Amended). The ~~conjugate~~ method of claim ~~17~~, wherein component (2) is hyaluronic acid or a salt thereof.

25 (Previously Presented). The method of claim 17, wherein the joint disease is selected from the group

consisting of osteoarthritis, rheumatoid arthritis, and scapulohumeral periarthrititis.

26 (New). The method of claim 24 wherein the hyaluronic acid has a weight average molecular weight of 100,000 to 10,000,000.

27 (New). The method of claim 11, wherein the site of the therapeutic agent for joint diseases is first bonded to the spacer and then the spacer is bonded to the carboxyl group of the hyaluronic acid, derivative or salt.

28 (New). The method of claim 11, wherein the binding reaction takes place in an aqueous solution containing 1 to 50% of an organic solvent.

29 (New). The method of claim 28, wherein the organic solvent is selected from the group consisting of N,N-dimethylformamide, N-methylpyrrolidone, dioxane, ethanol and pyridine.

30 (New). The method of claim 11, wherein said binding step further includes the addition of an additive for accelerating the binding reaction.

31 (New). The method of claim 30, wherein the additive for accelerating the binding reaction is selected from the group consisting of N-hydroxysuccinimide, N-hydroxy-5-norbornene-2,3-dicarboximide, p-nitrophenol, pentafluorophenol, 1-hydroxybenzotriazol and 1-hydroxy-7-azabenzotriazol.